VOLUME - 11, ISSUE - 04, APRIL - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Clinical Microbiology

A STUDY TO DETERMINE THE INCIDENCE OF BACTERIAL AND FUNGAL INFECTIONS IN ICU PATIENTS ON MECHANICAL VENTILATION AND ASSOCIATED OUTCOME

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ABSTRACT

Background: Infection in intensive care unit (ICU) patients, occurring predominantly in patients whose lungs are ventilated, at a rate of 1% to 3% per day of mechanical ventilation. Bacterial and fungal pathogens from clinical cultures were evaluated to characterize community- and ICU infections, including describing temporal changes in predominant organisms on presentation and throughout hospitalization.

Aims & objective: To determine the incidence of bacterial and fungal infections in ICU patients on mechanical ventilation.

Methods & materials: The study was Prospective observational case study was conducted at Medicine department in SRN Hospital, Prayagraj, U.P. India between July 2020 to June 2021. Endotracheal aspirates were collected aseptically from 100 ICU patients The various patient data such as age, gender, address, date of admission ,level of consciousness, risk factors involved, underlying diseases, duration of mechanical ventilation, prior antibiotic therapy etc. were recorded.

Result: In this study total 100 out of 81 patients show micro-organism infection, 76 patients had bacterial infections and 5 had fungal infections and 19 patients had no growth, as confirmed by endotracheal tube aspirate (ETA) culture growth.

Participants in the Bacterial group ETA Gram Staining was 38.2% had no abnormality detected (NAD), 52.6% had Gram Negative Bacilli and 9.2% of the participants had Gram Positive Bacilli, 100.0% of the participants in the Fungal group ETA Gram Staining had NAD. There was a significant difference between the various groups in terms of distribution of ETA Gram Staining ($\chi 2$ = 7.366, p = 0.028). In the Bacterial endotracheal tube (ET) aspirate culture 35.5% of the participants had *Klebsiella*, 25.0% had *Staphylococcus*, 18.4% had *E. coli*, 18.4% had *Pseudomonas*, 0.0% had *Candida* spp, 1.3% had *Acinetobacter*, 1.3% had *Proteus*. In the Fungal ET aspirate culture group 100.0% of the participants had *Candida* spp. There was a significant difference between the various groups in terms of distribution of ET aspirate: Culture ($\chi 2$ = 81.000, p = <0.001

Conclusion: Gram Negative Bacilli was the most common infection in patients on mechanical ventilation in gram staining. Klebsiella was the most common bacterial infection and Candida species was fungal infection. The poorest outcome occurred in patients with, *E. coli,* and *Proteus* group infection and good outcome occurred in *Acinetobacter*.

KEYWORDS : Infections, Endotracheal tube aspirate, Gram staining, Culture

INTRODUCTION

An infection is the invasion of an organism's body tissues by disease-causing agents, their multiplication, and the reaction of host tissues to the infectious agents and the toxins they produce.[1] Infections can be caused by a wide range of pathogens, most prominently bacteria and viruses.[2] The symptoms of an infection depend on the type of disease. Some signs of infection affect the whole body generally, such as fatigue, loss of appetite, weight loss, fevers, night sweats, chills, aches and pains.[3] Infections are among the most important causes of mortality worldwide and has plagued the low and lower middle countries more intensely.[4]

The intensive care units (ICUs) are often called "the hubs" of infections. Extremely vulnerable population group with reduced host defenses and dysregulated immune responses, multiple procedures, and use of invasive devices such as endotracheal intubation, central venous cannulations, mechanical ventilation (MV), and urinary catheterizations distorting the anatomical integrity protective barriers of patients are the important reasons.[5]

Both primary infections (at the time of admission) and secondary infections (occur during the stay in ICU or ICU acquired infections) rates are high in ICUs. In fact, ICU population has one of the highest occurrence rates of nosocomial infections (20–30% of all ICU admissions),[6] moved further and provided data and patterns of infections around the world including India.

Infections are caused by infectious agents (pathogens) including: Bacteria (*Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Escherichia coli*, *Clostridium botulinum*, and *Salmonella* spp.) Fungi, further sub classified into Ascomycota, including yeasts such as *Candida* (the most common fungal infection), filamentous fungi such as *Aspergillus*, *Pneumocystis* species, and dermatophytes, a group of organisms causing infection of skin and other superficial structures in humans.[7]

Infections were associated with Gram-positive isolates, and Gram-negative isolates. In patients with positive isolates, the most common gram-positive organism was *S. aureus* (20%), and the most common Gram-negative organisms were *Pseudomonas* species (20%) and *Escherichia coli* (16%) [8] Several studies show that Western ICUs have more Gram-positive organisms causing infections as compared to Asian ICUs including India, where Gram-negative infections are predominant.[9]

Bacterial and fungal infections in ICU are very common problem in India; studies are needed to record the incidence of bacterial and fungal infections in ICU patients on mechanical ventilation.

METHOD & MATERIALS

The study was Prospective observational case study was conducted at Medicine department in Swaroop Rani Nehru Hospital, Prayagraj, U.P. India between July 2020 to June 2021. The study was done in 100 patients on ventilatory support for more than 48hrs in the Medical Intensive Care Unit (MICU).

Inclusion Criteria:

- Age > 18 years.
- Patients undergoing mechanical ventilation for more than 48hrs, with the radiological and clinical parameters

indicative of Ventilator Associated pneumonia.

Exclusion Criteria:

- Severely Immuno-compromised states such as Acquired immune deficiency syndrome (AIDS), organ transplant patients, terminal stages of malignancy are excluded.
- Patients with pneumonia prior to mechanical ventilation or within 48 hours of Mechanical ventilation.

A detailed clinical history and clinical examination was carried out as per working proforma. The various patient data such as age, gender, address, date of admission, level of consciousness, underlying diseases, date of intubation/ tracheostomy, duration of mechanical ventilation, prior antibiotic therapy, routine investigation etc. were recorded. The clinical condition of patients was followed up from the time of inclusion in the study to the date of discharge from MICU unit.

Under strict aseptic precautions, samples were collected from the patients and transported immediately to the laboratory in appropriate settings and sample processing done. Microbiological culture analysis of endotracheal tube aspirate was preformed according to the CSLI method. Briefly, part of the Aspirates was subjected to Gram staining, and the rest of the samples were immediately incubated onto a blood agar plate, a MacConkey plate, and a chocolate agar plate. All cultures were incubated at 37° C under aerobic atmosphere. Cultures were evaluated for growth 24 hrs and 48 hrs later and discarded, if negative, 5 days after. The next day, aerobic cultures were examined for the growth of organisms. The plates which showed growth were studied by colony morphology, gram reaction and motility (hanging drop).

RESULT

Out of 100 patients, 81 patients show micro-organism infection, 76 patients had bacterial infections and 5 had fungal infections and 19 patients had no growth, as confirmed by ETA culture growth.

Table: 1 ETA culture growth: Infection Incidence of the study (n= 100)

ETA culture growth	Number of patients (n)	Percentage (%)
Bacterial	76	76%
Fungal	5	5%
No Growth	19	19%
Total	100	100%

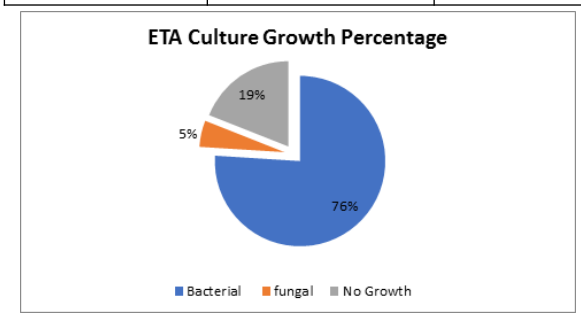

Figure 1

Table 2: Distribution of the cases in Terms of ETA: Gram Staining (n = 100)

ETA: Gram Staining	Frequency	Percentage	95% CI
NAD	53	53.0%	42.8% - 63.0%
Gram Negative	40	40.0%	30.5% - 50.3%
Gram Positive	7	7.0%	3.1% - 14.4%

The 53.0% of the cases had Gram Staining NAD and 40.0% of the cases had Gram Negative and 7.0% of the cases had Gram Positive.

There was a significant difference between the various groups in terms of distribution of ET aspirate Gram Staining ($\chi2$ = 7.366, p = 0.028).

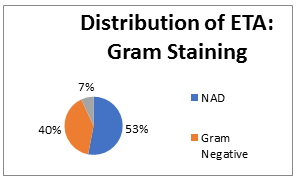

Figure 2

Table 3: Distribution of the cases in Terms of ETA: Culture (n = 100)

ETA: Culture	Frequency	Percentage	95% CI
No growth	19	19.0%	12.1% - 28.3%
Klebsiella	27	27.0%	18.8% - 37.0%
Staphylococcus	19	19.0%	12.1% - 28.3%
E. coli	14	14.0%	8.1% - 22.7%
Pseudomonas	14	14.0%	8.1% - 22.7%
Acinetobacter	1	1.0%	0.1% - 6.2%
Proteus	1	1.0%	0.1% - 6.2%
Candida spp	5	5.0%	1.9% - 11.8%

Total of the 19.0% of the participants had ETA Culture No growth, 27.0% Klebsiella, 19.0% Staphylococcus, 14.0% *E. coli*, 14.0% *Pseudomonas*, 1.0% of *Acinetobacter*, 1.0% *Proteus* and 5.0% of the participants had *Candida* spp.

There was a significant difference between the various groups in terms of distribution of ET aspirate: Culture ($\chi2$ = 81.000, p = <0.001

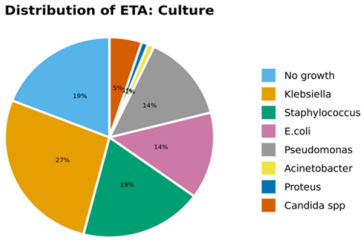

Figure 3

Table 4: Association Between ETA: Culture and Outcome (n = 100)

Outcome	ETA: Culture								Fisher's Exact Test	
	No growth	*Klebsiella*	*Staphylococcus*	*E. coli*	*Pseudomonas*	*Acinetobacter*	*Proteus*	*Candida spp*	Total	$\chi2$	P Value
Discharged	12 (63.2%)	11 (40.7%)	11 (57.9%)	0 (0.0%)	5 (35.7%)	1 (100.0%)	0 (0.0%)	2 (40.0%)	42 (42.0%)	17.958	0.002
Expired	7 (36.8%)	16 (59.3%)	8 (42.1%)	14 (100.0%)	9 (64.3%)	0 (0.0%)	1 (100.0%)	3 (60.0%)	58 (58.0%)		
Total	19 (100.0%)	27 (100.0%)	19 (100.0%)	14 (100.0%)	14 (100.0%)	1 (100.0%)	1 (100.0%)	5 (100.0%)	100 (100.0%)		

Cases in the ETA Culture with *Acinetobacter* had the largest proportion of Outcome with Discharged, and in *E. coli*, and *Proteus* had the largest proportion of Outcome was Expired. There was a significant difference between the various groups in terms of distribution of Outcome ($\chi2$ = 17.958, p = 0.002).

DISCUSSION

In study, there were total 100 cases, out of them 81 patients

show micro-organism infection, 76 patients had bacterial infections and 5 had fungal infections and 19 patients had no growth, as confirmed by ETA culture growth. *Chelazzi C et al*[10] studied on 494 patients admitted to the ICU, 46 (9.3 %) acquired an infection 48 or more hours after admittance. *Vadivoo N et al*[11] study showed that a total of 95 endotracheal isolates were processed and 73 % of the aspirates were showing growth. The incidence of VAP was 33.3%. *Thongpiyapoom S. et al*[12] in their article stated that incidence of VAP varying from 3.5 to 46 per 1000 ventilator days. Different study showed the different rate of incidence of infection in intubated patient, in this study the incidence of infection was 81%. This was depending on epidemiology of infection in that particular area and septic precaution taken during intubation and in management of patients and nursing care.

In this study, on Gram staining of ETA, 53.0% of the participants had NAD and in 40.0% were Gram Negative and 7.0% of the participants were Gram Positive. *Chelazzi C et al*[10]study showed that' in 30/46 patients (65.2 %) the isolated bacterium was Gram-negative. *Richa Gupta et al*[13] studied on the Gram-negative bacteria comprised 68 (88.3%) of the total isolates, among which 49 (72.1%) were multidrug-resistant (MDR). Gram-positive organisms comprised four (5.2%) of the total isolates and all four (100%) were MDR. *Aspergillus fumigates* (6.4%) was the only fungal pathogen identified. *Pseudomonas* was the predominant pathogen associated with VAP. *Vadivoo N et al*[11] study showed that the incidence of VAP was 33.3% and most frequently isolated pathogens were *Klebsiella* spp (36%), *Pseudomonas* (17%) & *Acinetobacter* spp (18%). Different study showed that gram negative bacterial infection was most common in intubated patients and in gram negative infection *Klebsiella* was the most common bacteria associated with ventilator associated pneumonia. So all of the above study favored this study that gram negative bacteria was the most common bacteria associated with ventilator associated pneumonia in which *Klebsiella* was the most common gram negative bacteria.

Study showed on culture of ETA, 19.0% of the cases had No growth and in 27.0% of the cases ETA Culture showed *Klebsiella* and in 19.0% showed *Staphylococcus* and 14.0% showed *E.coli* and in 14.0% of the cases ETA Culture had *Pseudomonas* and 1.0% of the cases had *Acinetobacter* and in 1.0% had *Proteus* and in 5.0% of the cases had *Candida* spp. There was High Strength of association between the two variables (Cramer's V) = 1. *Vadivoo N et al*[11] studied on 95 endotracheal isolates were processed and 73 % of the aspirates were showing growth. The incidence of VAP was 33.3% and most frequently isolated pathogens were *Klebsiella* spp (36%), *Pseudomonas* (17%) & *Acinetobacter* spp (18%). *Terraneo S et al*[14] studied on 385 consecutive immune competent patients were assessed with ICUAP, according to the presence or absence of *Candida* spp. in lower respiratory tract samples. *Candida* spp. was isolated in at least one sample in 82 (21%) patients. *Chakraborti A et al*[15] study showed that Long-term mechanical ventilation (>7 days) is strongly associated with fungal colonization of the respiratory tract and urinary tract. *T E.Meawed et al*[16] study showed that All specimens of 197 critically ill COVID-19 patients under mechanical ventilation 197/197 (100%) were positive for bacterial infections, while fungal elements were detected in 134/197 (68%) of specimens. The most frequently isolated bacteria were pan drug resistant (PDR) *Klebsiella pneumoniae* (41.1%), followed by multi drug resistant (MDR) *Acinetobacter baumannii* (27.4%). On the other hand, *Candida* species represented the most frequently isolated fungi (75.4%) followed by molds including *Aspergillus* (16.4%) and *Mucor* (8.2%) species. *Chun-Yu Lin et al*[17] study showed that Twenty-five (80.6%) patients were diagnosed as having proven IFT and the remaining patients had probable IFT. *Aspergillus* spp. (61.3%) was the most common pathogenic species, followed by Mucorales (25.8%) and *Candida* spp. (6.5%). *M. T. Montagna et al*[18] studied that the main infections were caused by yeasts, more than filamentous fungi (overall incidence of 16.5 cases per 1,000 admissions and 2.3 cases per 1,000 admissions, respectively). So all of the above study in bacterial culture of endotracheal aspirates showed that *Klebsiella pneumoniae* was the most common bacterial infection VAP and in Fungal infection *Candida* infection was most common cause in patients on ventilator. And all of these result favored this study that *Klebsiella pneumoniae* was the most common infection in bacterial culture. And in fungal culture 100 % of patients had *Candida* spp infection. *M. T. Montagna et al*[18] study showed that the overall crude mortality rate was high (42.8 %), particularly for mold infections (61.5 %). All yeast infections were *Candida* bloodstream infections. *Malini R et al*[191] study showed that all patients with mould infections expired before the mycological culture results. *Zhang Y et al*.[20] revealed in their paper that a study in India on HAP that found an overall crude mortality of 67.4% in ICU patients with pneumonia, with 40% of the mortality in these patients attributable to infection alone. This study showed that percentage mortality was maximum in *E. coli* group followed by *Klebsiella* after that Fungal VAP.

CONCLUSION:

In this study the incidence of infection in ICU patients on mechanical ventilation was 81%. The incidence of bacterial infection in ICU patients on mechanical ventilation was 76 %. The incidence of fungal infections in ICU patients on mechanical ventilation was 5%. In this study, Gram Negative Bacilli was the most common infection in patients on mechanical ventilation in gram staining. In gram negative, *Klebsiella* was the most common bacterial infection. In fungal culture, *Candida* species was most common fungal infection. This study concluded that the poorest outcome occurred in patients with, *E. coli,* and *Proteus* group infection in which 100.0% of participants were expired. Infection with good outcome occurred in *Acinetobacter*, in which 100% of patients were discharged.

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